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10/692,684	10/27/2003	Tetsuya Suga	242791US0CONT	2064

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.  
1940 DUKE STREET  
ALEXANDRIA, VA 22314

EXAMINER	
BRANSON, DANIEL L	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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patentdocket@oblon.com  
oblonpat@oblon.com  
jgardner@oblon.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/692,684	<b>Applicant(s)</b> SUGA ET AL.
	<b>Examiner</b> DANIEL L. BRANSON	<b>Art Unit</b> 1616

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 April 2011.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 12-17, 19-36, 38-46, 48-53 and 75-78 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 12-17, 19-36, 38-46, 48-53 and 75-78 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br/>Paper No(s)/Mail Date <u>05/26/2011</u>.</p> | <p>4) <input type="checkbox"/> Interview Summary (PTO-413)<br/>Paper No(s)/Mail Date. _____.</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application</p> <p>6) <input type="checkbox"/> Other: _____.</p> |
|---|--|

## **DETAILED ACTION**

### ***Status of Application***

Claims 1,12-17, 19-36, 38-46, 48-53, and 75-78 are pending. Claims 1, 22, 36 and 42 are currently amended.

Receipt and consideration of Applicants amendments and remarks filed on April 21, 2011 and the § 1.132 affidavit filed on April 21, 2011 is acknowledged.

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are reiterated. They constitute the complete set of rejections presently being applied to the instant application.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 1,12-17, 19-36, 38-46, 48-53, and 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchiyama et al. (US 2002/0119164 (of record)) in view of Kropf et al. (US 6,858,214 (of record)) and Desai et al., Gastrointestinal Uptake of biodegradable microparticles: Effect of particle size, Pharmaceutical Research, Volume 13. No. 12, 1996 (of record).**

### **Applicant Claims**

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Applicant claims a composition comprising superfine particles of a  $\beta$ -glucan derived from a water extract of a mushroom, wherein the superfine particles have an average particle diameter of 10 $\mu$ m or less, as determined in the form of a dispersion in water.

Applicant also claims a process for producing superfine particles comprising superfine pulverizing a  $\beta$ -glucan derived from a water extract of a mushroom.

### **Determination of the scope and content of the prior art**

#### **(MPEP 2141.01)**

Uchiyama et al. teach *Agaricus blazei* (a mushroom) in whole, particulate, or extracted form, can be used to treat forms of damage to the skin caused by toxins and chemicals (see the abstract and page 2 paragraph 25). *Agaricus blazei* (a mushroom) in whole, particulate, or extracted form, when taken internally, also offers protection against various disorders including autoimmune disorders (see the abstract and page 2 paragraph 26). The identified compounds that have been extracted from *Agaricus blazei* and that are of particular use in the invention include beta glucans (see page 3 paragraph 34 and claims 1 and 12).

The extraction may be done by immersing the mushroom in particulate form, in an aqueous solution or parts thereof with The extraction can also be done by immersing particulate *Agar/ous blaze/*, in plain hot water, preferably over 90°C (see page 2 paragraph 32 and page 3 paragraph 33). The extract may be freeze dried or concentrated using water or methanol/acetone solutions (see page 3 paragraph 33). The ratio of mushroom to water is preferably between 1:2

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and 1:100 (see page 3 paragraph 33). The concentration of the extract is preferably between 0.05% and 50% v/v (see page 3 paragraph 44).

The extract can be used with other active or inactive ingredients and can be formulated as a liquid, capsule, pill, tablet, solution suspension or emulsion (see page 4 paragraphs 45 and 51). The extract can be formulated as a solution by dissolving the *Agaricus blazei* extract in water, oils, propylene glycol, etc. (see page 4 paragraphs 45 and 51 ). A wide variety of agents may be added to produce better dispersions or to accentuate cooling, soothing, or protective properties.

The extract is useful for treating skin disorders and internal diseases such as autoimmune diseases topical or internally (orally) (see page 3 paragraphs 37- 43 and page 4 paragraphs 48-49). The extract may treat diabetes, lupus, certain types of cancer and can be used in the form of a food, drink or dietary product (see page 4 paragraph 50).

### **Ascertainment of the difference between the prior art and the claims**

#### **(MPEP 2141.02)**

Uchiyama et al. teach the *Agaricus blazei* extract (i.e. beta glucans) can be present in particulate form but do not teach the particle size of the extract. Uchiyama et al. also do not teach lecithin. These deficiencies are cured by the teachings of Kropf et al. and Desai et al.

Kropf et al. disclose the use of nanoscalar water-soluble 13-glucans. The 13- glucans are contained in cosmetic and/or pharmaceutical preparation having particle diameters in the range of 10 to 300 nm (equivalent to 0.01 to 0.30  $\mu\text{m}$ ) (see column 1, lines 43- 47). The composition can further contain adjuvants known in the cosmetic and/or pharmaceutical industry (see column

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3, lines 19- 34). Column 5, lines 51-52 teach that lecithin can be used in the composition as a hyperfatting agent.

Desai et al. teach the effect of particle size on the gastrointestinal uptake of biodegradable microparticles. In general, the efficacy of uptake of 100nm size microparticles by the intestinal tissue (e.g. Peyer's patch) was 15-250 folds higher when compared to large size microparticles. This is particularly important in the design of oral drug delivery systems (see the abstract).

### **Finding of prima facie obviousness**

#### **Rational and Motivation (MPEP 2142-2143)**

One of ordinary skill in the art would have been motivated to formulate the *Agaricus blazei* extract (i.e. beta glucans) with the instant particle size (i.e. 10 $\mu$ m or less) because the instantly claimed beta glucans are known for use topically to treat skin conditions and orally in pharmaceutical formulations. It is well known in the art to formulate beta glucans with the instantly claimed particle size for cosmetic or dermatological purposes, as suggested by Kropf et al. Further, it is known in the art that using a smaller particle size (e.g. 100nm) can increase the efficacy and delivery of the active to the intestinal tissue, as suggested by Desai.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate the *Agaricus blazei* extract (i.e. beta glucans) with the instant particle size (i.e. 10 $\mu$ m or less) because it is an obvious particle size that beta glucans can be prepared when used for pharmaceutical or cosmetic purposes. And further, because it will result in enhanced uptake of active, resulting in improved bioavailability and enhanced drug

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absorption, and reduced toxicity.

Although Uchiyama et al. do not teach lecithin can be used in the formulations, it is a common and known hyperfatting agent (emulsifier) that can be used in formulations containing beta-glucan, as suggested by Kropf et al. Thus, it would have been obvious for one of ordinary skill in the art to incorporate lecithin into the formulation taught by Uchiyama et al., because it is a common additive to add to formulations depending on the desired form of the final product.

With respect to claims 39 and 44, although Uchiyama et al. do not specifically teach the step of filtering the extract, it would have been obvious to one of ordinary skill in the art to filter the extract, so as to remove any excess solution, impurities or additional materials that are not needed in the extract.

With respect to claims 16-17, it is also noted that the reference does not teach that the product can be made by the process instantly claimed, i.e. filtering, filtering and then concentrating and/or cooling. However, the patentability of a product does not depend on its method of production. If the product in the product-by-process claims is the same or obvious from a product in the prior art, the claim will be held unpatentable even if the prior product is made by a different process (See MPEP 2113).

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

### **Response to Arguments**

Applicant's arguments filed April 21, 2011 have been fully considered but they are not persuasive. Applicant argues that the primary reference Uchiyama et al., is overly generic and does not actually disclose or suggest that the water extract of mushroom *Agaricus blazei* contains any  $\beta$ -glucans, nor that the specific fractions containing  $\beta$ -glucans could or would be used for any specific purpose.

This argument is not persuasive for three reasons. First, Uchiyama et al. specifically teaches that extracts of *Agaricus blazei* are preferably prepared using "water extraction" or more preferably "hot water extraction" (see paragraphs 32 and 33). Identified compounds in polar solvent extracts include beta-glucans (see paragraph 34). Thus, it would have been obvious to one of ordinary skill in the art to try water extraction or hot water extraction to obtain beta glucans since they are preferred methods in obtaining the polar solvent extracts of identified compounds (i.e. beta glucans). Second, water is a more polar solvent than methanol, thus hot water extracts of *Agaricus blazei* would necessarily contain  $\beta$ -glucans which contain many polar hydroxyl groups. To provide additional evidence/basis in fact to demonstrate that hot water extracts of *Agaricus blazei* inherently and necessarily contain beta-glucans as asserted, the Patent Examiner cites the article entitled "Structural characterization of a water soluble  $\beta$ -D-glucan from fruiting bodies of *Agaricus blazei* Murr" by Dong et al. Dong et al. teach  $\beta$ -D-glucan was obtained in a hot-water (100 °C) extract of the fruiting bodies of *Agaricus blazei* Murr and then further isolated by ethanol precipitation, anion-exchange and gel-permeation chromatography (abstract, page 1420, paragraphs 4-6). As Uchiyama teaches the hot water extraction protocol on *Agaricus blazei* preferably uses water which is above 90 °C and up to 100 °C, the extract



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obtained thereby would necessarily contain  $\beta$ -glucans as indicated by Dong et al. Thus, Uchiyama necessarily teaches a composition comprising particles of a  $\beta$ -glucan derived from a water extract of a mushroom. Third, Applicant has chosen to claim the invention as a composition and a method of making that composition, not a method of using the composition. Thus, arguments alleging that Uchiyama et al. do not suggest a specific purpose for the  $\beta$ -glucans are irrelevant. After giving the Applicant's claims their broadest reasonable interpretation, no intended use is required by the limitations of the claims. Even if the claims did require the composition to be used for a specific purpose, Uchiyama et al. teach that their hot water extract of mushroom, which would necessarily comprise  $\beta$ -glucan as established above, can be used topically to prevent and treat damage to skin such as skin cancers and can be taken internally to treat or prevent disorders such as diabetes.

Applicants further argue that Kropf et al. teach the particle size of a yeast extract of beta-glucans and not mushroom extracts of beta-glucans, and thus is related to a different invention. Applicant argues that beta glucans extracted from yeast are structurally different. Applicant has provided references to establish that beta glucans derived from yeast are structurally different from beta glucans extracted from mushrooms. Applicant has further provided a declaration from Yasuyo Suga where Yasuyo has opined that because of the differences in structure between the  $\beta$ -glucans derived from mushrooms and yeast, a skilled artisan would not modify a disclosure of  $\beta$ -glucans from one based on a disclosure of  $\beta$ -glucans from the other.

Applicant's argument of non-analogous art is not convincing. First and foremost, Applicant claims a  $\beta$ -glucan derived from a water extract of a mushroom, without limiting to a  $\beta(1\rightarrow6)$  glucan. The attempt to distinguish the  $\beta$ -glucan structurally by source additionally fails

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because Applicant cannot prove hot water extracts of mushrooms are void of  $\beta(1\rightarrow3)$  glucans, the type of  $\beta$ -glucans found in yeast. Indeed, one of the references that Applicant has provided to this Office states in part, "Primarily,  $\beta$ -1,3-glucan is the major component of oats, mushrooms and yeasts" ('Potentiation of intestinal immunity by micellary mushroom extracts' by Shen et al). Thus, trying to distinguish the reference based upon structure fails. Furthermore, the expert opinion of Yasuyo Suga sets forth facts which are incomplete with the prior art as cited above by ignoring the fact that a major component of the  $\beta$ -glucans of both mushrooms and yeast are  $\beta(1\rightarrow3)$ glucans. Thus, the opinion and conclusion derived therefrom is found unpersuasive.

Even if the claim had limited the  $\beta$ -glucan to a  $\beta$ -(1 $\rightarrow$ 6)-glucan,  $\beta$ -glucans from both mushrooms and yeast are known in the art to possess immune modulation activities. A skilled artisan looking to enhance the absorption, bioavailability and degree of immune activation of and by a mushroom  $\beta$ -glucan would have been motivated to look to at least the prior art of  $\beta$ -glucans, regardless of source, to obtain a solution to the enumerated problems to be solved and would have found Kropf et al. Although Kropf et al. teach that the beta glucans are prepared from a yeast extract, the end result is the same. In both references, the beta glucans are being used for the same purpose and in the same type of formulations. It would have been obvious to one of ordinary skill in the art to try to prepare the beta glucans taught in Uchiyama et al. within the same particle size range as instantly claimed (i.e. less than 10 microns) because it has been disclosed by Kropf et al. that beta glucans can be used effectively in cosmetic and pharmaceutical formulations when prepared within the instantly claimed particle size range (i.e. less than 10 microns). Furthermore, while Applicant has repeatedly pointed out that some yeast and mushroom  $\beta$ -glucans differ structurally, they have failed to provide evidence that these

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structural differences actually make the mushroom  $\beta$ -glucans less suitable for forming superfine particles utilizing the method of Kropf et al which would discourage a skilled artisan from relying on Kropf et al. to solve these problems. Indeed, such a showing would be difficult in the light of the fact that the method of Kropf et al. is very similar to that of Applicant used to prepare the instantly claimed particles of  $\beta$ -glucan derived from a water extract of a mushroom. Finally, it is known in the art that a smaller particle size (e.g. 100 nm) has a higher efficiency of uptake when compared to larger particle sizes, as suggested by Desai. The particulate carrier system is important for oral drug delivery in order to enhance absorption and bioavailability.

Next the Applicant defers to three declarations in order to attempt to establish non-analogous art as well as secondary considerations/unexpected results in which to overcome the present *prima facie* case of obviousness. Each of the three declarations will be discussed below in turn and conclusions regarding probative value regarding the establishment of unexpected results and non-analogous art are reiterated from past office actions as well as issued de novo.

### **Consideration of §1.132 Declarations**

A Declaration is reviewed for at least the following: 1) whether there is a nexus between the merits of the claimed invention and the evidence of secondary considerations (*Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 USPQ 657,673-674 (*Fed. Cir.* 1985)), 2) whether the declaration compares the claimed subject matter with the closest prior art (*In re Burckel*, 201 USPQ 67 (CCPA 1979)), 3) whether the objective evidence of non-obviousness is commensurate in scope with the claims which the evidence is offered to support (*In re Clemens*, 206 USPQ 289, 296 (CCPA 1980)), 4) whether the Declaration shows a difference in kind rather than merely a difference in degree (*In re Waymouth*, 182 USPQ 290, 293 (CCPA 1974)), and 5)

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whether the record establishes such a strong case of obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness (*Newell Cos. V. Kenney Mfg. Co.* 864 F.2d 757, 769; *Richardson-Vicks, Inc., v. The Upjohn Co.*, 122 F.3d 1476, 1484). The Patent Examiner must also determine whether the evidence shows unexpected results (MPEP 716.02(a)).

Applicant has submitted a § 1.132 declaration on September 23, 2009. Applicant compared a beta-glucan solution wherein beta-glucan has an average diameter of about 200 microns, a beta-glucan solution wherein beta-glucan has an average diameter of about 100 nm (instant invention), and a control where no beta-glucan is used. The compositions were evaluated for incorporation (absorption) into the small intestines Peyer's patch. The composition of the instant invention (solution of beta-glucan with a particle size of about 100 nm) had the highest absorbability.

First, it should be noted that figures 1, 3, 5 are not visible and figures 2, 4, 6 are not in color. And thus, one of ordinary skill in the art cannot visibly and accurately ascertain whether any unexpected results have occurred with respect to the photographs.

Second, Applicants have not compared their invention with the closest prior art, but rather with beta-glucan particle of a 200 micron diameter. Thus, with no gauge of how absorption into peyer's patches was different from that of the closest prior art, unexpected results cannot be ascertained.

Finally, Applicant is purporting that the use of beta-glucans with a superfine particle size resulted in a higher absorbability. However, this result is not unexpected. It is known in the art that particle size plays a role in the gastrointestinal uptake of drugs or carriers and the use of

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smaller “superfine” particle sizes (e.g. 100 nm) will lead to an increase in uptake of particles in tissues, such as Peyer’s patch, when compared to the use of larger particles sizes (as evidenced by Desai et al.). Thus, it is not unexpected for a solution containing beta-glucan at a particle size of 100 nm to be absorbed by the intestinal tissue in a greater amount when compared to the beta-glucan solution having a beta-glucan particle size of 200 microns.

Applicant has submitted another two § 1.132 declarations on September 27, 2010 and April 21, 2011. It should be noted these declarations consist of opinion. Opinions directed to legal conclusions are not considered and are given no weight whereas opinions directed to technical data are considered but given reduced weight.

In the declaration of September 27, 2010, Applicant has given an opinion that a skilled artisan would not modify a disclosure of  $\beta$ -glucans from mushrooms based on a disclosure of  $\beta$ -glucans from yeast. The opinion is based on the fact that there are various types of  $\beta$ -glucans, and there are differences in structure between  $\beta$ -glucans from mushrooms and those from yeast. Applicant argues that mushrooms, but not yeast, contain  $\beta$ -1,6-glucans. To support the proposition that mushrooms contain  $\beta$ -1,6-glucans, Applicant cites 5 articles that study separately the compositions of three different mushrooms, *Lentinula edodes*, *Schizophyllum commune* and *Sclerotium*. Applicants cite several entries from [wikipedia.org](http://wikipedia.org) as well as two other references to show that yeast comprise mostly  $\beta$ -glucans having 1,3 linked main chains and partly having 1,6 linked branched chains and that mushrooms comprise the 1,6 linked main chains, not the 1,6 linked branched chains.

The Patent Examiner, after considering this portion of the Declaration and articles, accepts at face value that mushrooms contain some  $\beta$ -glucans which yeast do not. That some  $\beta$ -

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glucans are different between the different sources, however, is not the end of the inquiry.

Investigation must also be made into the portion of  $\beta$ -glucans which are similar or the same between the different sources. Indeed, Applicant admits that both yeast and mushrooms contain  $\beta$ -1,3-glucans in the present Declaration (see page 2, paragraph 1) and has presented a reference to this Office in this Declaration that says in part, "Primarily,  $\beta$ -1,3-glucan is the major component of oats, mushrooms and yeasts" ('Potentiation of intestinal immunity by micellary mushroom extracts' by Shen et al). Thus, as the prior art is clear that a majority of  $\beta$ -glucans in mushrooms and yeast are  $\beta$ -(1,3)-glucans, the Declarants conclusion of non-analogous art based upon incomplete facts is given reduced weight.

The declarant further asserts that there is no direct relationship between the absorbability and the medical effect of  $\beta$ -glucans and points to two Suga et al. and one Shen et al. reference to support this proposition. Possible explanations are given for why particle size is not always directly related to absorbability and immune activation by the active agent. Despite the previous declaration's lack of evidence as to medical effect or immune activation induced by the particle, Declarant then concludes that the absence of a direct link between absorbability and the medical effect of  $\beta$ -glucan proves that the results demonstrated in the previous Declaration (which increased absorbability) are unexpected.

The Patent Examiner has reviewed both of the Suga et al references as well as the Shen et al. reference. The only reference which provides objective evidence to support the Applicants conclusion that absorbability/size of the  $\beta$ -glucan is not directly related to the medical effect thereof is the Suga et al. reference published in 2005. In Suga et al (2005), it was demonstrated that oral administration of M-LNT and MME particles approximately 0.4 microns in diameter

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induced anti-tumor activity, while L-LNT of approximately 130 microns and S-LNT of an unmeasurably small diameter did not (the latter which was presumed to be absorbed in the GI tract because of its small diameter). The Patent Examiner finds this objective evidence as an indication of unexpected results regarding medicinal effects of the particle size of M-LNT as compared with similarly prepared, but larger/smaller diameter L-LNT and S-LNT.

This objective evidence, however, must be considered in light of factors 2) and 3) *supra*. Suga et al. (2005) does not compare M-LNT against the closest prior art. Thus, with no gauge of how the medical effect of certain sized particles was different from that of the closest prior art, unexpected results cannot be ascertained in this regard. Furthermore, Suga et al's objective evidence of non-obviousness is not commensurate in scope with the claims which the evidence is offered to support. The independent claims of issue require that the particles of  $\beta$ -glucan are less than 10 microns. Suga et al (2005) clearly demonstrates that not all particle less than 10 microns exhibit a medical effect. It is difficult to ascertain where the line is drawn, as the smallest particle that exhibited no medical effect has an undetermined diameter. Nonetheless, the claim limitation regarding particle size is much broader than the 0.4 micron diameter which has been demonstrated to have unexpected results in Suga et al (2005).

It should also be noted that the assertion made in the first Suga declaration regarding the exertion of an inhibitory effect on tumor growth being dependent on particle diameter, and that smaller particle size is absorbed into peyer's patch and larger particles are not is completely at odds with the assertion in the second Suga declaration that there is no direct relation between particle size, absorption and medical effect of the  $\beta$ -glucan particle.

Applicant filed a third Declaration on April 21, 2011. Essentially the results of Suga et al. (2005) were outlined and Dr. Okumura concluded that a correlation between the particle size and the effects of  $\beta$ -glucan cannot be predicted and would not have been expected. In order to avoid duplicity, the Patent Examiner directs the Applicant's attention to the above discussion of Suga et al. (2005) which addresses the salient points of this third Declaration.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Patent Examiner should be directed to DANIEL L. BRANSON whose telephone number is (571)270-3812. The Patent Examiner can normally be reached on M-F 7-3:30.



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If attempts to reach the Patent Examiner by telephone are unsuccessful, the Patent Examiner's supervisor, Johann R. Richter can be reached on (571)272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel L. Branson

/Johann R. Richter/  
Supervisory Patent Examiner, Art Unit 1616